CASE REPORTS

Intracranial Metastases of Primary Pulmonary Carcinoma: A Diagnostic Difficulty

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ERRORS in clinical diagnosis are most often referable to the fact that the particular disease of the patient is not considered by the clinician. Secondly, errors are sometimes made because certain conditions simulate each other and the secondary effects overshadow the real nature of the illness. It is inevitable that clinical errors usually are most apparent in retrospect and that the true extent of the difficulties during the course of the patient's illness is obscured by the definitive findings at necropsy.

The difficulties in the differential diagnosis between primary intracranial neoplasms and secondary intracranial growths, particularly in bronchogenic carcinoma, are well recognized. Carcinoma of the lung metastasizes to the brain more frequently than neoplasms of other portions of the body. Necropsy material reveals intracranial metastases in 15 to 30 per cent of cases of pulmonary carcinoma;[6,8,14] metastases to the brain in other forms of cancer occur in about 1 per cent of the cases.[6] Of metastatic brain tumors, approximately 50 per cent have the primary source in the lung.[10] Bronchogenic cancer probably reaches the central nervous system by way of the blood stream. Cell emboli from pulmonary tumors may thus pass from the pulmonary vein and heart directly into the general and the cerebral circulation, whereas similar emboli from elsewhere in the body on their way to the central nervous system have to pass through the pulmonary circulation and are retained in the sieve of the pulmonary capillaries.

Clinically, 60 to 70 per cent of patients with bronchogenic carcinoma have symptoms suggesting pulmonary disease.[9,14] The clinical picture in about 10 per cent of the cases is that of an intracranial lesion.[1,15] The problem of differentiating primary brain tumors and brain tumors metastatic from primary pulmonary carcinoma is encountered approximately 1700 times each year in the United States, considering that some 175,000 people die of cancer annually, and that about 10 per cent of these have cancer of the lung.[15] A report on 448 cases of pulmonary cancer at the Mayo Clinic[16] states that 52, or 12 per cent of the patients, had symptoms referable to the central nervous system. In 19 cases the initial and predominant symptoms were those of brain involvement, and in eight cases a localized brain lesion was suspected; two patients underwent exploratory craniotomy.

The difficulties that are encountered in some of these cases[4,8,10,13,16] are well illustrated in the reports of two patients observed at the Tumor Clinic, Marine Hospital, Baltimore*. Even a cranial operation did not clarify the diagnoses in these cases, and the records would have shown them as brain tumors if necropsy had not been performed.

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CASE 1

A 54-year-old Norwegian longshoreman was admitted to the hospital with the chief complaint of recurrent convulsive seizures.

Present Illness: Thirteen months before admission, the patient had had a convulsive attack, during sleep, characterized by loud grunting respirations, foaming at the mouth, turning of the head to the right, and spasmodic movements of the extremities. He had had six similar nocturnal seizures at monthly intervals. About 20 minutes before the attacks the patient had marked generalized headache. The convulsions, sometimes accompanied by vomiting of a projectile type, and more recently by incontinence of urine and feces, lasted a few minutes and were followed by a period of unconsciousness lasting up to three hours. After the attacks there were persistent headache and backache, which were accentuated by stooping. The convulsions gradually became more frequent and marked and occurred during the day as well as at night. Progressive dimness of vision developed in the left eye, with loss of memory, general deterioration, and loss of strength.

Past History: The patient's mother and three siblings died of pulmonary tuberculosis. The patient had had a cough with whitish sputum for the past three weeks but denied other pulmonary symptoms. During the past year he had gained 65 pounds over his normal weight of 185 pounds.

Physical Examination: The patient was well-developed, obese, and did not appear ill. The temperature, pulse, and respirations were normal. The vision in the left eye was destroyed except for an island through which only form could be distinguished, above and to the right of the macula in the field. There were bilateral retinochoroiditis and incipient cataracts; there was no papilledema. The lungs were normal except for harsh breath sounds and occasional dry rales over the right apex posteriorly. The heart was normal; the blood pressure was 150 mm. systolic and 88 mm. diastolic. The abdomen, genitalia, and the extremities were normal. Result of examination of the nerve system was essentially negative.

Laboratory Findings: The blood and the urine were normal. Results of the Kline and Eagle tests were negative. Spinal puncture showed the fluid to be under a pressure of 320 mm. of water. The fluid was xanthochromic, contained 107 mg. per cent of protein, and was slightly turbid. Pandy test showed 4 plus. Kahn test was negative, and the gold curve was 11111. Another spinal puncture done ten days later showed the fluid to be under a pressure of 250 mm. water. The fluid was clear with negative Kahn and Eagle tests, a flat gold curve, and no increase in globulin.

A roentgenogram of the chest showed a mottled infiltration throughout both lungs, the greatest change radiating laterally to the right lung root area. These changes were reported as strongly indicating a tuberculous infection.

A ventriculogram showed air in both lateral ventricles. Both ventricles of the brain were slightly enlarged, and there was a prominence seen in the upper wall of the left ventricle which projected downward. An encephalogram also demonstrated this defect. An electroencephalogram study indicated

that a space-occupying process in the left frontal region was likely.

Course: The patient had a convulsion two weeks after entry. It began with loss of consciousness and deep respirations, followed by tenseness of the body and slight clonus. Both arms were rigidly fixed and jerky, and there was carpopedal spasm. The eyes were turned to the right and the pupils were widely dilated. The patient voided involuntarily.

The convulsion, during which the patient became cyanotic, lasted about three minutes. However the patient was not able to respond to questioning until a half-hour later.

Craniotomy was performed six weeks after entry. When the dura was opened the cortex was pale and there was slight increase in intracranial pressure. A needle introduced into the superior frontal gyrus to a depth of 1 cm. entered a cavity which contained a large amount of liquefied blood. The cavity was evacuated after incision and washed out with saline.

Histologic examination of a small bit of tissue removed at operation showed it to be a piece of cortex in which was embedded a piece of tissue composed of papillary epithelium lined by tall, columnar cells with suggestion of mucus formation (Figure 1). It was felt that this was probably a metastatic papillary carcinoma, possibly from the lung. After considerable study, however, this impression was changed to a papilloma of the choroid plexus, similar to the cases described by Van Wagenen.[17] Consultation with an authority on this type of neoplasm produced the following statement: "The tumor is a perfectly benign growth of the choroid plexus and represents in all probability a fragment of papilloma. There is no question in my mind that it is not a pulmonary carcinoma."

A month after operation the patient had another convulsion, and an attempt to remove the brain tumor was made. It was found that the cyst had not recurred. In its place there was definite solid tumor tissue, which was exposed and was found to extend backward under the motor cortex. A considerable amount of the tumor was removed. Histologic examination of the mass revealed an appearance seen previously. Diagnosis of papilloma of the choroid plexus was reiterated.

The patient recovered from the operation and was discharged. However, he continued to have convulsive seizures and gradually became more somnolent, apathetic, and deteriorated. Roentgen therapy over the head was started in an attempt to alleviate the convulsive seizures. Under this therapy and phenobarbital, the patient's condition appeared to become quiescent. Repeated roentgenograms of the chest showed slow, slight increase in the density of the numerous areas of infiltration seen previously. One area extending laterally from the right lung root shadow was approximately 3x5 cm. in size (Figure 2). The patient's course continued slowly downhill. He died following a convulsion from which he did not recover consciousness, 13 months after his initial entry to the hospital and 26 months after his initial convulsive seizure.

Clinical Impression: Papilloma of choroid plexus. Pneumoconiosis or tuberculosis of lungs.

Necropsy: The ventricles of the brain were dilated, and the corpus callosum was markedly thinned. There was no tumor in either of the lateral ventricles, and the choroid plexus appeared normal. The left hemisphere, at a section passing through the genu of the corpus callosum, showed a major defect 4 cm. in diameter, communicating with the cortex superiorly and opening into the anterior pole of the left lateral ventricle. The walls of this cystic cavity were irregular in contour, granular, and yellowish. There were solid nodular areas in the grey matter of the insula, and in the grey matter of the parietal lobe near the sagittal sulcus. Similar tumor areas 1 to 5 cm. in diameter were also encountered in the nucleus ruber, the parietal occipital region, and the superior portion of the occipital lobe. The right hemisphere of the brain had a large cystic cavity 5 cm. in diameter occupying most of the frontal lobe. It communicated with the right lateral ventricle. There were numerous small areas of tumor in the cortex of the right hemisphere in a section passing through the optic chiasm, and in the cortex from here to the occipital end of the brain. In the white matter of the occipital pole was a nodule 2 cm. in diameter.

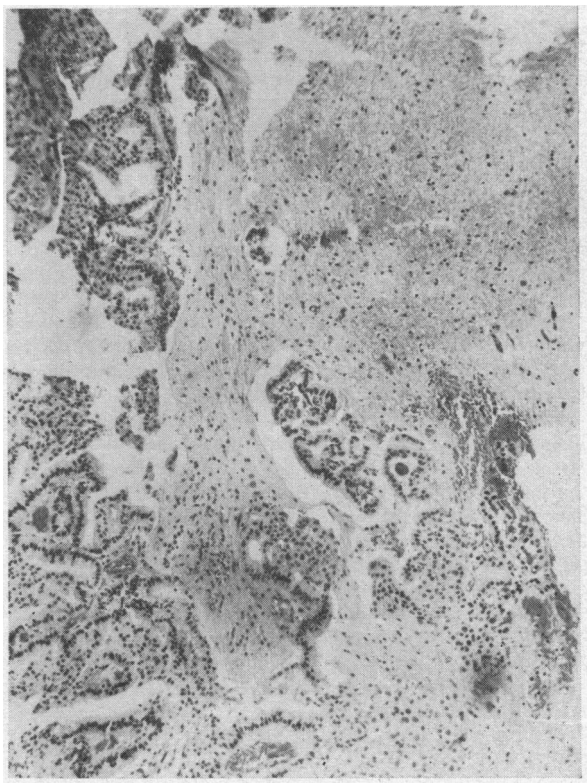

Figure 1.—Case 1 (M. J.). Section of tumor removed from the brain, showing a papillary growth that was mistaken for a papilloma of the choroid plexus. Haematoxylin and eosin (x 150).

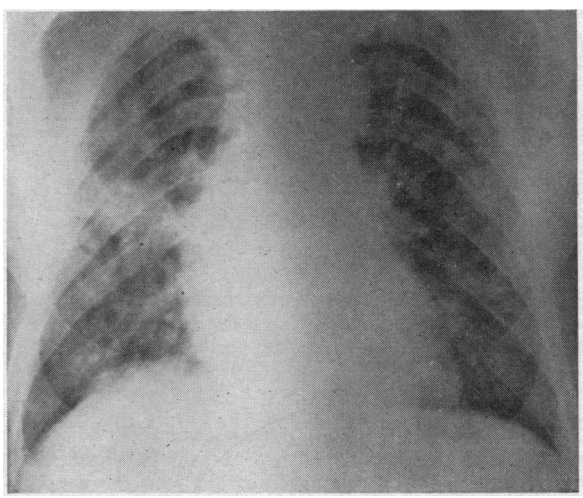

Figure 2.—Case 1 (M.J.). Roentgenogram of chest (January 2, 1942), showing diffuse mottled infiltrations throughout both lungs and a density extending from the right lung root.

The left pleural cavity was free of adhesions, but over the surfaces of the parietal pleurae there were small, firm, white nodules attached to the pleural surfaces. These nodules were up to 5 mm. in diameter and were arranged linearly along the intercostal spaces. The right pleural cavity was adherent over its total surface, and in the superior mediastinum there was a large fibrous mass, 5 cm. in diameter, which was attached on one side to the pericardium and on the other to the hilar surface of the right lung. The mass was firm and showed small areas of calcification. There were a few scattered calcified areas in the neighborhood of the mass in the lung tissue.

Both lungs showed firm nodules scattered irregularly throughout the upper and lower lobes. On cut section these were well-circumscribed, rubbery areas, 1 to 2 cm. in diameter, which were not associated with the bronchi.

Microscopic examination of the choroid plexus revealed a perfectly normal structure covered by a single layer of uniform cuboidal cells with eosinophilic cytoplasm. There was some superficial resemblance between the choroid plexus and the papillary projection seen in this tumor, in that the cells of the tumor were cuboidal, showed a regular single cell layer and eosinophilic cytoplasm. In some areas, however, the epithelium of the tumor showed a tendency to produce mucin and form granules. In one of the small brain metastases, the tumor was much more solid and in some areas appeared to be an epidermoid carcinoma.

Microscopic examination of the white nodules in the left pleural cavity revealed that the major portion of these nodules was composed of a dense collagenous tissue. At the base of this connective tissue, however, there was evidence of tumor in the form of alveoli and glandlike arrangements. The nodules in the lung were also composed of tumor, of the same papillary type but more tightly packed. In addition, there were areas of the lung in which solid masses of tumor were present within the alveoli and showed the pavementlike arrangement of epidermoid carcinoma (Figure 3).

Metastases of the tumor were present in the hilar lymph nodes, the liver, and the kidneys.

Final Diagnosis: Carcinoma of the lung with metastases to the pleura, liver, kidneys, lymph nodes, and brain.

COMMENT

The symptoms and signs in the patient were primarily referable to the brain. The patient had a strong family history of tuberculosis. The only chest symptoms were a slight cough and production of whitish sputum for three weeks before admission. He did not produce sputum and was afebrile during the course of his illness at the hospital. The patchy, multiform areas of consolidation revealed in the roentgenograms of the chest appeared to be stationary upon repeated examinations. These facts led to the misinterpretation of the lesions as an old, quiescent, tuberculous infection.

Any possible connection between the pulmonary findings and the cranial lesion was hopelessly confounded by the erroneous histologic diagnosis of the brain tumor tissue. The first diagnosis of metastatic carcinoma was changed to papilloma of the choroid plexus and was backed by an authority on the latter type of tumors. The true nature of the process was not clarified until complete necropsy had been performed.

CASE 2

A 53-year-old white marine engineer was admitted to the hospital with the chief complaints of weakness, headaches, and progressive impairment of vision.

Present Illness: About five months previously the patient noticed that he was forgetful and that he began to have trouble with men working under him. Finally he had a "nervous breakdown." He felt dizzy, had right-sided headaches with occasional diplopia, nausea, and vomiting. His vision became progressively dimmer. He had no paralyses or paresthesias and no convulsions or periods of unconsciousness.

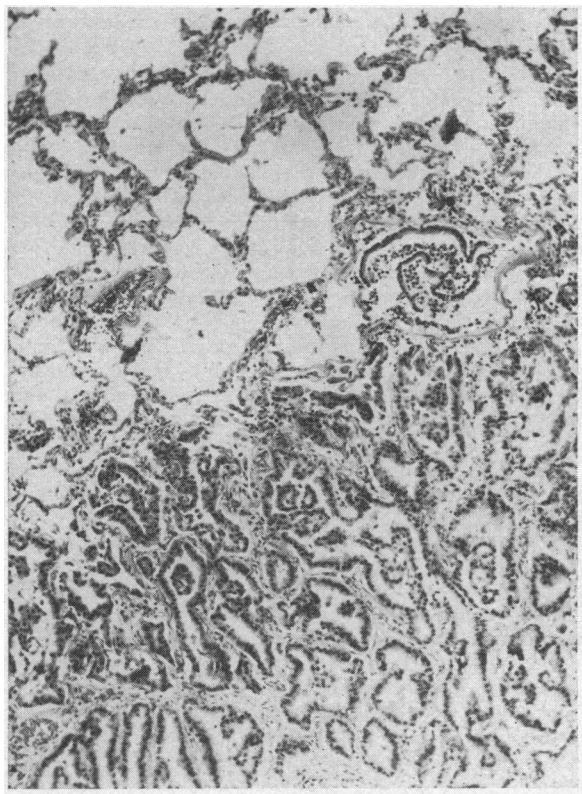

Figure 3.—Case 1 (M. J.). Primary papillary carcinoma of the lung. Haematoxylin and eosin (x 150).

The condition of the patient deteriorated steadily. His wife described him as being abnormally quiet, very slow in his movements, gloomy, and negativistic. He could not remember recent events and complained of double vision and headaches. During his illness the patient had lost 40 pounds in weight, from over 200 to 160 pounds.

Past History: The patient's mother had died at age 37 of pulmonary tuberculosis, and his father at age 60 of heart disease. Three siblings were living and well. He had had no visual complaints until the present illness. About a year before admission, he was on a boat torpedoed at sea, and after being adrift for five days was rescued and taken to Africa. While there, the patient had had a protracted febrile disease, stated by the patient to have been malaria. He denied night sweats, cough, sputum, or hemoptysis.

Physical Examination: The patient was well developed, fairly well nourished, and appeared to be chronically ill. The temperature, pulse, and respirations were normal. The skin had many dry scales and pigmented nevi characteristic of ichthyosis.

The patient was able to distinguish fingers at 20 feet. There was right hemianopsia of both eyes and a convergence paralysis. There was paresis of the left medial and right superior recti. Papilledema was present on the left side. The tongue protruded to the right, and a slight tremor was present. The chest was normal to inspection, percussion, and auscultation, as were the heart and the abdomen. Blood pressure was 130/88. Rectal examination revealed a slightly enlarged prostate.

Examination of the nervous system showed that the right side of the face and body were weaker than the left. The gait was unsteady, and Romberg's sign was present, with the falling to the right. The deep reflexes on the right were diminished. Right abdominal and cremasteric reflexes were not obtained, and there was a Babinsky reflex on the right side. The position sense of the right leg and foot was impaired.

The speech was slow and halting; the patient forgot complete sentences, and his immediate memory was poor. He was oriented to time and place.

Laboratory Findings: The urine and the blood were normal, the results of Kline and Eagle tests negative.

A roentgenogram of the chest showed an area of density without any borders, which extended upward from the right lung root and involved the lower medium half of the upper right lobe. No changes were seen above the shadow of the clavicle, and the margins faded out gradually (Figure 4). The findings were interpreted to indicate the presence of moderately advanced pulmonary tuberculosis.

An encephalogram showed a large defect in the region of the left lateral ventricle which deformed both the upper and lower sections of this ventricle and also displaced it to the right side. There was also some displacement of the right lateral ventricle.

Clinical Impression: Malignant brain tumor of left temporal-parietal region. Pulmonary tuberculosis of right upper lobe.

Course: The patient underwent craniotomy one week after entry. The brain was under marked tension, and there was some herniation of the cortex when the dura was opened. Several centimeters below the cortex a large infiltrating tumor was encountered, extending deep into the midline. A large portion of the infiltrating mass was removed.

Pathologic examination of a number of sections taken from various portions of the tissue showed a large amount of tissue which was uniform in structure and appeared to be composed chiefly of fibroglia fibers with a rather even distribution of astrocytes. The tissue contained moderate-sized areas of hemorrhage and small areas of calcification; there were also small areas of inflammation. The diagnosis of fibrous astrocytoma was reported.

The patient recovered from operative shock, but his general condition remained poor. He was aphasic and had complete paralysis of the right arm. Three days post-operatively he developed an area of consolidation at the left lung base and expired in coma two days later, about six months after the onset of the initial symptoms.

Necropsy: Significant findings were limited to the head and thorax. The skull was considerably thinned out, more so on the left than on the right, and in the temporal region in some places was about 1 mm. in thickness. There was a large hemorrhagic and necrotic process involving an area of about 8 cm. in diameter in the left temporal and parietal region. The vessels at the base of the brain, the pituitary gland, and the dural sinuses were normal.

The right pleural cavity showed old fibrous adhesions over the apex; the left pleural cavity was free of adhesions. The posterior and inferior portions of both lungs revealed nodular consolidation and large amounts of fluid and blood, and small amounts of purulent material were expressed from the cut sections of these areas. In the apex of the right lung there was a gelatinous consolidation studded with chalky white areas. In conjunction with this process was an old area of cavitation about 2 cm. in diameter.

Microscopic examination of the large hemorrhagic, necrotic mass in the brain revealed no evidence of glioma. There were numerous areas in which the brain tissue was markedly changed, and there were areas of gliosis, which undoubtedly led to the erroneous diagnosis of astrocytoma. In the most posterior portion of the hemorrhagic area, there was a large tumor nodule composed of necrotic, metastatic carcinoma. The area was at least 3 cm. in diameter.

Microscopic examination of the nodular areas in the apex of the right lung revealed nests of tumor cells which had abundant eosinophilic cytoplasm with sharply marked cytoplasmic boundaries. In some areas the nests of cells were arranged in a pavementlike pattern. Between these nests of

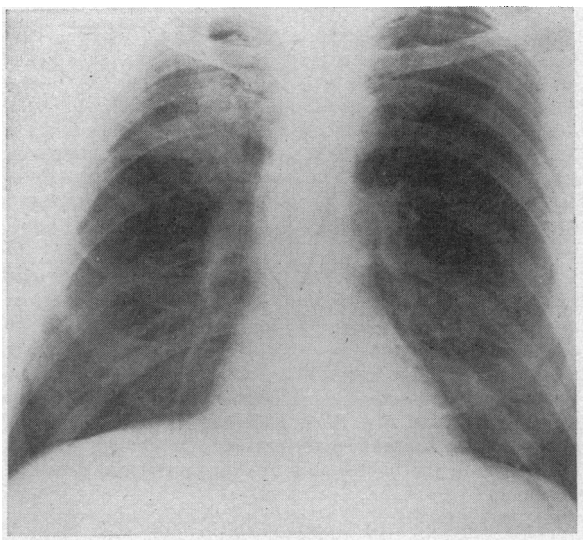

Figure 4.—Case 2 (J. C. B.). Roentgenogram of chest (December 6, 1941), showing a density without borders in the right upper lobe, extending upward from the right lung root.

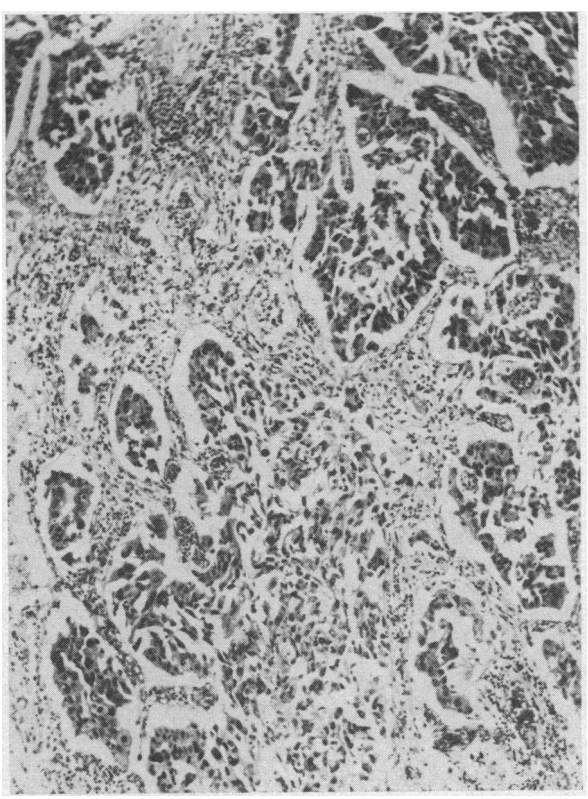

Figure 5.—Case 2 (J. C. B.). Primary epidermoid carcinoma of the lung. Haematoxylin and eosin (x 150).

cells there was a considerable degree of fibrosis, and the areas as a whole were walled off by a heavier wall of fibrous connective tissue (Figure 5). There was widespread confluent bronchopneumonia. There was no evidence of tuberculous infection.

Final Diagnosis: Epidermoid carcinoma of the right lung, with metastasis to the left cerebral hemisphere; terminal bronchopneumonia.

COMMENT

The symptoms and signs in this case were limited to the brain. The patient had a family history of tuberculosis, but otherwise no indication of a pulmonary lesion was present until the roentgenogram of the chest was obtained. It was felt in retrospect that the roentgenogram should have led to a greater consideration of a primary pulmonary carcinoma, since it revealed a unilateral density near the hilus ramifying into the parenchyma in a man of 53, whose clinical course was afebrile and without other evidence of pulmonary tuberculosis.

The chief confusion, however, arose because the glial reaction of the cerebral tissue was interpreted as caused by an astrocytoma, rather than by metastatic carcinoma. Such reactions to metastatic lesions are encountered frequently, the response being much like that found in wounds and infections of the brain.[8] As in the first case, this led to the erroneous clinical and gross pathological diagnosis and a discounting of the pulmonary process—errors that were not rectified until the microscopic examination of the tissues at necropsy.

DISCUSSION

The clinical diagnosis of primary pulmonary carcinoma in a patient with symptoms and signs of a brain lesion is based upon suspicion and upon verification of the suspicion. Fried and Buckley[8] believe "that when a person of middle age has an abrupt onset of symptoms and signs of a rapidly developing intracranial lesion, a metastatic cerebral lesion should be thought of, and that the lungs are the most common site of the primary lesion."

The age and the mode of onset of symptoms, however, are not clear indications. About 10 per cent of bronchogenic carcinomas occur in individuals under 40 years of age,[14] and the onset of cerebral symptoms may be quite gradual. It is apparent that it should be a routine procedure to obtain roentgenograms of the chest, as well as to attempt to rule out other neoplastic foci, in all patients suspected of having a primary neoplasm of the central nervous system.

The symptoms, signs, structure of tissue, and other features of primary carcinoma of the lung have been the subject of numerous excellent papers and monographs and need no reiteration here. In the 10 per cent of cases in which the presenting symptoms of the disease are those of intracranial disturbance, roentgenograms of the chest are usually the first and the chief diagnostic aid. The roentgenographic features of pulmonary carcinoma vary greatly, and roentgen examination does not establish a definite differential diagnosis even in extensive involvements,[2] but the roentgenogram does show the presence of a lesion in over 95 per cent of the cases.[18]

The presence of a lesion in the lungs of a patient with manifestations of an intracranial process should indicate a further and exhaustive investigation of the intrathoracic findings.

Further roentgenographic studies, such as exposures from several angles, and fluoroscopy, are useful particularly in the case of lesions at the root of the lung. Special techniques, particularly bronchography with the aid of iodized oil,[7] and tomography,[20] are often valuable. Demarcation of peripheral masses may be facilitated by roentgenograms following artificial pneumothorax.

Examination of the sputum or of pleural exudate may reveal the diagnosis by the demonstration of neoplastic cells. Wandall[19] found cells of malignant tumors in the sputum of 84 of 100 patients with bronchogenic carcinoma, and Herbut and Clerf made the finding in 22 of 30 such patients. The presence of tubercle bacilli does not rule out carcinoma, as Brunn[3] reported this organism in 10 per cent of 626 patients who had pulmonary carcinoma.

The bronchoscope is an invaluable instrument in the examination of the respiratory tract. Jackson[12] stated that bronchoscopic examination and biopsy will establish the diagnosis in about 75 per cent of the cases. Direct aspiration biopsy may be helpful in peripheral lesions not accessible to the bronchoscope.[5]

It has been stated[4,8] that when a single tumor in the brain is the only demonstrable metastasis and the primary pulmonary carcinoma is slowly growing, enucleation of the cerebral lesion has led to prolongation of the patient's life and to relief of suffering caused by the expanding intracranial lesion. At least the prolongation of survival has been questioned;[16] the length of life of these patients is approximately six months after onset of symptoms.

SUMMARY

The diagnostic problem of differentiating intracranial metastases of primary pulmonary carcinoma and primary intracranial neoplasms is illustrated by a review of two cases.

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Friedlander Bacillus Meningitis

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FRIEDLANDER bacillus meningitis is rare. Thirty-three cases have been reported in the literature.[4, 6, 8, 9] In a recent report, Pain and his co-workers[7] note a case of Friedlander bacillus, type A, meningitis, with the organism secured from cerebrospinal fluid, blood and aural discharge. The patient received sulfadiazine, penicillin, and streptomycin, but died 33 hours after the first dose of streptomycin. In almost all cases there has been coincidental septicemia, and almost all the patients have died. The disease was found to originate in the lung in five of 29 cases reviewed by Ransmeier.[8] In 1943, 51 cases of primary Friedlander bacillus pneumonia were reported,[5] and among them were two cases of Friedlander bacillus meningitis secondary to Friedlander pneumonia.

CASE REPORTS

CASE 1. The patient (Case 9 of the Friedlander pneumonia series)[5] was a 52 year old white male. He entered the hospital in a preterminal comatose state, and died in seven hours. Friedlander bacilli, type A, were cultured from the sputum, blood, and cerebrospinal fluid. The patient had pneumonia involving the right upper lobe and the left lower lobe, and also meningitis. He died without receiving any specific therapy. (Pre-chemotherapy era.) At autopsy, pneumonia and purulent meningitis were the chief findings. Postmortem cultures of the lung, meninges, and spleen were positive for Friedlander bacilli, type A.

CASE 2. The patient (Case 50 of the Friedlander pneumonia series)[5] was a 37 year old white male. He entered the hospital acutely ill, with cough and thick, tenacious, mucopurulent, blood streaked sputum. Examination and a chest roentgenogram revealed pneumonia of the entire left lung and, in addition, signs of meningitis were present. Friedlander bacilli were cultured from the sputum, blood and cerebrospinal fluid. No typing of the organism was done. The patient died on the fourth hospital day after an acute toxic course. No chemotherapeutic or anti-biotic agents were available (1935). Postmortem examination revealed a Friedlander pneumonia and purulent meningo-encephalitis. Postmortem cultures of the heart, lung, blood, spleen and meninges were positive for Friedlander bacilli.

As in most of the reported cases of infection with Friedlander bacilli, neither of the patients received specific therapy. Two patients given sulfonamides are reported to have recovered.[8, 9] One patient treated with streptomycin died, but "the absence of gross and the nearly complete absence of microscopical evidence of meningitis at autopsy are stressed."[9] Experimental evidence indicates that both sulfadiazine[1] (Table 1) and streptomycin[2, 3] are effective in vitro against certain strains of Friedlander bacilli, although not against all.

TABLE 1.—*Mice Survival and Chemotherapy*

(Adapted from Feinstone, Williams, Wolff, Huntington, and Crossley[1])

	No. of Mice	Mice Surviving	Per Cent Survival
Sulfanilamide	100	2	2.0
Sulfapyridine	99	6	6.0
Sulfathiazole	100	2	2.0
Sulfadiazine	86	63	73.6
Controls	78	0	0.0

Heilman[2] studied nine strains. Four of these, type A, had not been recently isolated. Five strains had been recently isolated, but were not type A or B. All nine strains were sensitive to streptomycin in vitro, the recently isolated strains being more sensitive. Using a single strain of Friedlander bacilli sensitive to streptomycin, Heilman found that in mice inoculated intra-abdominally with 10,000 times the lethal dose of bacilli, streptomycin given three hours after the inoculation and then for a total of three days, would give complete protection. The control mice, not receiving streptomycin, were all dead within one day. Similar experiments in which mice were inoculated intra-abdominally with 1,000 times the lethal dose of a type A strain of Friedlander bacilli, and then were treated with streptomycin suspended in oil and beeswax, produced essentially similar results. When the mice were infected by intranasal doses of Friedlander bacilli type A, the protection given by streptomycin was less, although here too the drug was of definite value. The mortality rate for streptomycin-treated intranasally infected mice (seven days of therapy) was 13 per cent compared with 100 per cent for the control group. It is important to stress that streptomycin was given very soon (three hours) after the introduction of the Friedlander bacilli (Table 2). It is clear that adequate therapy had best include both sulfadiazine and streptomycin, to be given promptly and in adequate doses, and to be pursued vigorously. These drugs can be of value only before suppuration, or at least extensive suppuration, has begun. Their greatest value is, of course, at the onset of the disease. The importance of an adequate and intensive early search for bacterial invaders (smears and cultures of sputum and cerebrospinal fluid and blood cultures) is clear.

SUMMARY AND CONCLUSIONS

1. Two cases of Friedlander bacillus meningitis are reported. Both patients died, one in seven hours and one on the fourth hospital day. Sputum, blood, and cerebrospinal fluid cultures were positive for Friedlander bacilli in both cases. Neither patient received chemotherapeutic or antibiotic agents, as these were not available at the time.

2. Friedlander bacillus meningitis should be treated promptly with sulfadiazine and streptomycin, since these drugs have been shown to have value, both in vitro and in vivo.

ADDENDUM

Since this report was submitted, S. S. Jacob and F. H. Top (Annals of Internal Medicine, 28:1003-1009, May, 1948) have reported seven cases of Friedlander bacillus meningitis with two recoveries. The patients who recovered had negative blood cultures and both seemed to be helped by sulfadiazine and penicillin.

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